

**A PROSPECTIVE OBSERVATIONAL STUDY OF LEVELS OF SERUM LDH
AND ITS CORRELATION WITH FETOMATERNAL OUTCOME AND
SEVERITY IN HYPERTENSIVE PREGNANT WOMEN**

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AIM:

- a)To compare the severity of hypertensive disorder of pregnancy with respect to their serum LDH levels.
- b)To study the fetomaternal outcome of woman with raised LDH levels.

METHODS:

It was a prospective observational study of the levels of serum LDH in hypertensive pregnant women and their fetomaternal outcome in women with HDP admitted in labour room of tertiary health care centre of South Gujarat for 1 year period after official approval from Ethics Committee.100 consecutive consenting intranatal women with HDP admitted in labour room of New Civil Hospital were enrolled in this study.

RESULTS:

41% of the subjects had gestational hypertension,38% had pre-eclampsia(8% non severe while 30% had severe pre-eclampsia),17% of the subjects had eclampsia and only 4% had pre-eclampsia superimposed on chronic hypertension.The mean serum LDH of our study was 498.66U/L.70% of the subjects belong to the age group 20-29yrs.57 subjects were multipara.61% of the subhects were registered antenatally .66 subjects delivered beyond 36 weeks of gestation.71 subjects underwent LSCS while rest were delivered vaginally.40 subjects had maternal complications, 36 neonates required NICU admission and there were 6 still births.

CONCLUSION:

Preeclampsia and its complications significantly contributes to maternal and perinatal mortality and morbidity. Timely intervention and management can prevent the complications. From this study, after analysing the data, it is found that there is increase in severity as well as increase in incidence of maternal and perinatal complications with increase serum Lactate dehydrogenase levels in HDP. Thus it is concluded that serum lactate dehydrogenase which is an early marker of hypoxia at cellular levels, can be used as a biochemical marker to assess the severity of the disease and to predict the complications in all HDP patients. Thereby, close monitoring and early intervention and prompt management of the HDP patients with

elevated serum LDH levels can prevent complications and thereby helps to improve the maternal and perinatal outcome in HDP.

INTRODUCTION:

Hypertension is one of the most common medical complications during pregnancy. Hypertensive disorders of pregnancy complicates 5-10% of pregnancies worldwide and increasing incidence due to , women are postponing their first pregnancy to later age and increased pre pregnancy weight. Hypertensive disorders remain one of the leading causes of maternal and perinatal morbidity and mortality.

There is a system wide endothelial leak in pre-eclampsia and contributes to potentially lethal complications like eclampsia, placental abruption, DIC, acute renal failure, pulmonary edema and hepatocellular necrosis. Early recognition of women at risk of pre-eclampsia will help to identify the high risk women and the timely diagnosis and intervention may prevent complications and improve the pregnancy outcome. Defective trophoblastic invasion and widespread vasospasm and endothelial dysfunction are the main pathophysiology in development of pre-eclampsia. Pre-eclampsia is a multisystem disorder and leads to a lot of cellular death and LDH is a biomarker of cellular death and infact the earliest marker seen in blood during hypoxia and oxidative stress.

Serum LDH level reflects extent of cellular death and thereby the severity of pre-eclampsia and its level might be a guideline for management of patients. This study is an attempt to find out the role of serum LDH in prediction of adverse outcome of pre-eclampsia, severity of disease and occurrence of complications, both maternal and fetal.

This will help us know the outcome of the mother and the baby and our intervention at the earliest might be able to save lives and give a better prognosis to both mother and baby.

MATERIALS AND MEHODS:

DESIGN OF STUDY : Prospective observational study

PLACE OF STUDY:

Department of Obstetrics and Gynaecology, Government Medical College and New Civil Hospital, Surat.

STUDY POPULATION:

The Study group consists of hypertensive pregnant women who are admitted in the department of obstetrics and gynecology, at Government medical college and hospital, Surat

SAMPLE SIZE : 100 participants

INCLUSION CRITERIA:

100 consenting intranatal patients with hypertensive disorder admitted in labour room and delivered at NCHS having:

- Gestational hypertension
- Non severe pre eclampsia
- Severe pre eclampsia

- Eclampsia
- Pre eclampsia superimposed on chronic hypertension

EXCLUSION CRITERIA :

- Non consenting intranatal patients with hypertension
- Patients with chronic hypertension
- Delivery outside NCHS
- Patients having co-morbidities like DM,liver disease lung disease.

METHODOLOGY :

Informed consent was obtained from the patients. Detailed history including age, parity, previous medical disorders was elicited followed by physical examination including the measurement of blood pressure in the right arm, in sitting position with appropriate size cuff. Based on inclusion and exclusion criteria 100 intranatal mothers with hypertension were subjected to the study. Routine workup and management of all these subjects were done as per standard departmental protocol.

All data related to clinical profile, socioeconomic profile, investigations including serum LDH, fetomaternal outcome, any intranatal or postnatal complication (pulmonary edema, intracranial hemorrhage, abruption of placenta, ARF , PPH , mode of delivery, need for OBICU admission, baby weight, APGAR , NICU admission of enrolled subject were collected from the case record in a structured proforma and analysed with various statistical tests.

RESULTS:

Out of 100 subjects studied, distribution of subjects on the basis of severity of hypertension is as follows.

TABLE NO.1. Severity of hypertensive disorder with respect to LDH level

Severity of hypertension	LDH(<360U/L)	LDH(360-600U/L)	LDH(>600U/L)	Total
Gestational hypertension	10	27	4	41
Pre-eclampsia	6	23	9	38
Eclampsia	3	8	6	17
Pre-eclampsia superimposed on chronic hypertension	0	3	1	4
Total	19	61	20	100

Out of the 100 subjects ,41 had gestational hypertension, and their mean serum LDH value was 447.26U/L, 38 had pre-eclampsia with their mean serum LDH value being 504.86,17 had eclampsia and their mean serum LDH value was 581.88U/L.

We studied the association of serum LDH valu with severity of pre-eclampsia and we found the following.

Fig 2.Severity of pre -eclampsia with respect to LDH level

Severity of pre-eclampsia	LDH<360U/L	LDH >360U/L	P value
Non-severe	5	3	
Severe	1	29	0.003
Total	6	32	
SIGNIFICANT			

Yates corrected chi-square value is 12.48 and mid P exact value is 0.0003. P value <0.05 is significant. This shows that there is significant association between severity of pre-eclampsia and LDH value.

We also tried to establish any association with the registration status of the subjects and their serum LDH values, and found the following results.

TABLE NO 3.Mean LDH values with respect to registration status of the subjects

Registration status	Mean LDH value(U/L)
Registered (61)	450.06
Referred(35)	582.71
Emergency(4)	504.25

The mean LDH value of the registered subjects (61) was 450.06U/L,while that of the referred subjects was 582.71U/L and that of the emergency subjects was 504.25U/L.

This suggests that the referred and emergency hypertensive patients have higher LDH values, this suggests that antenatal patients having adequate number of antenatal visits decreases her chances of having higher LDH values , in later pregnancy.

The p value using the t test is 0.006,and the t test value is 2.18 which is significant,thus the registered patients have less mean serum LDH.

FETOMATERNAL OUTCOME:

As we analyze the maternal complications ,many subjects were found to have more than one complication.

TABLE NO.4.Maternal complications

Complications	LDH(<360U/L)	LDH (360-600U/L)	LDH(>600 U/L)	TOTAL
Maternal ICU admission	0	11	18	29

Hypertensive retinopathy	0	2	3	5
HELLP Syndrome	0	6	5	11
DIC	0	1	3	4
Abruptio placenta	0	2	4	6
Eclampsia	3	8	6	17
Postpartum hemorrhage	0	3	3	6
Pulmonary edema	0	2	3	5
Acute renal failure	0	0	2	2
Maternal death	0	0	2	2
Total	3	35	49	

There were total 40 subjects who had complications.

There were few subjects who had more than 1 complication which can be described below.

There were 28 subjects who had single maternal complication of hypertensive disorder of pregnancy, 7 subjects who had 2 maternal complications while only 5 who had 3 maternal complications combined.

Catazerite et al found in their study that group of women who had elevated serum LDH developed HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count) which is comparable to our study.

Therefore there is significant increase in incidence of complications and maternal morbidity in those with elevated serum LDH levels which is also comparable to the study conducted by Martin et al.

As one subject might have had more than 1 complication, we tried to analyse the number of complication with their mean serum LDH values.

Table 5. Number of maternal complications with the mean serum LDH values

The mean values of serum LDH in subjects having only one complication of hypertension in pregnancy was 588.60 U/L, while the mean value of serum LDH in subjects having 2 maternal complications was 666.85 U/L, while those having 3 complications their mean serum LDH was 926.20 U/L.

The p value using the t test is 0.006 which is significant, thus there is significant association between number of complications with serum LDH value.

No of maternal complications	Mean LDH values(U/L)
1	588.60
2	666.85
3	926.20

TABLE 6: Comparison of presence of maternal complications with levels of serum LDH.

Maternal complications	LDH<360U/L	LDH360-600U/L	LDH>600U/L	TOTAL	P value
Present	3	19	18	40	
Absent	16	40	4	60	0.00001
Total	19	59	22	100	
SIGNIFICANT					

In our study of 100 hypertensive patients we found that 40 of them had maternal complication while 60 of them did not have any maternal complication. P value using chi square test is 0.00001538 and the chi square value is 22.17. P value<0.05 indicates significance, which leads us to conclude that there is significant association between raised serum LDH values and presence of maternal complications. It is comparable to the study by Bhave et al⁷⁹ and Prajapati et al⁵³. Out of 102 neonates born(2 twins),there were 36 neonates who had complications and required NICU admission.

TABLE NO.7.Indication for NICU admission.

Indication for NICU admission	No of neonates
Prematurity	16
Low birth weight	19
IUGR	3
Birth asphyxia	8
Neonatal jaundice	8
TGA	1
Meconium stained liquor	6

16 neonates were premature requiring NICU admission with low birth weight,3 neonates were full term LBW i.e.IUGR.8 had neonatal jaundice,and 6 had meconium stained liquor out of which 6 developed asphyxia. 2 had only birth asphyxia due to other reasons and 1 had TGA.

TABLE NO.8.Comparison of serum LDH values with mean gestational age of the subjects at the time of delivery.

Perinatal outcome	LDH(<360U/L)	LDH(360-600U/L)	LDH(>600U/L)
Mean gestational age (wks) at the time of delivery	37.45wks	36.25wks	34.5wks

Mean birth weight(kgs)	2.50kg	2.45kg	1.985kg
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Out of 100 subjects,

- The subjects who had their serum LDH values < 360 U/L, their mean gestational age at the time of delivery was 37.45 wks
- The subjects who had their serum LDH values 360-600 U/L, their mean gestational age at the time of delivery was 36.25 wks
- The subjects who had their serum LDH values > 600 U/L, their mean gestational age at the time of delivery was 34.50 wks.

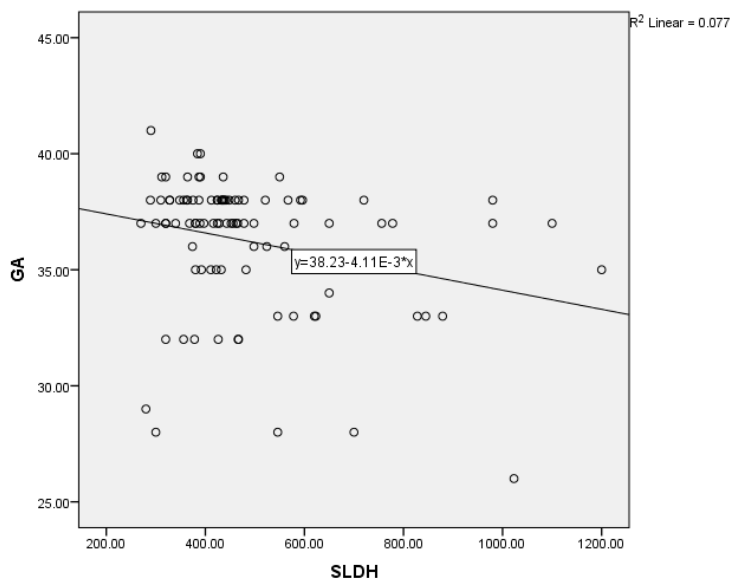
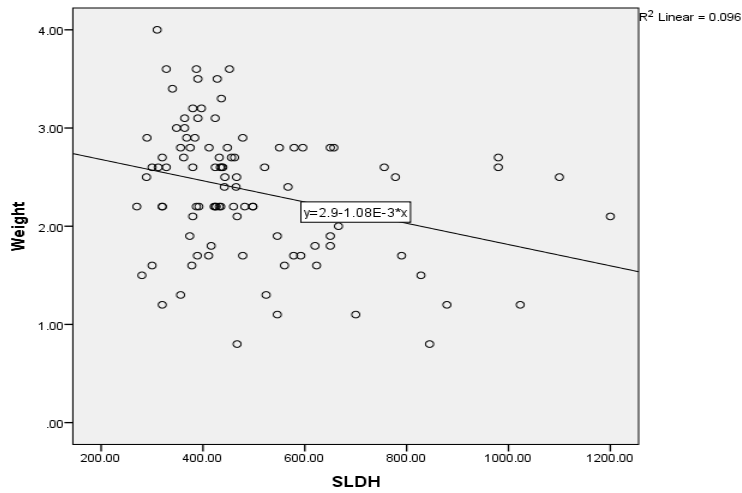
We also studied the correlation of serum LDH values with the gestational age in weeks at the time of delivery and found the following result.

Descriptive Statistics			
	Mean	Std. Deviation	N
SLDH	498.6600	189.06753	100
GA	36.1800	2.79747	102
Weight	2.3308	.65996	102

This is descriptive statistics table showing the mean values of serum LDH and gestational age at the time of delivery.

This table shows the correlation between serum LDH and birth weight of neonates is -0.3, and the p value of this correlation is 0.002 which is significant, suggesting that there is significant moderate negative correlation between S.LDH and birth weight of neonates.

Fig1 Correlation of serum LDH with birth weight of neonates and gestational age at delivery.



This table shows that the correlation between serum LDH and gestational age is -0.278, and the p value of this correlation is 0.005 that is significant. This suggests that there is significant weak negative correlation between serum LDH and gestational age at the time of delivery.

DISCUSSION:

The mean age group of subjects in our study was 25.4 years. The youngest subject was 17 yrs of age and the eldest was 42 yrs of age.

43% of subjects in our study were primipara, and 57% were multipara.

There is no association between serum LDH and parity in our study.

In our study 61% of the subjects were registered, 35% were referred and 4% were emergency.

The mean serum LDH value in unbooked subjects (referred = 582.71 U/L, emergency = 504.25 U/L) were greater as compared to the booked subjects (450 U/L) and the mean difference is significant (p value = 0.006).

Our study suggests that the referred and emergency hypertensive patients have higher LDH values, so antenatal patients having adequate number of antenatal visits(registered) decreases her chances of having higher LDH values , in later pregnancy,and better prognosis of both mother and baby,and any intervention if needed at the earliest.

Majority of the patients in our study were gestational hypertension(41%),and pre-eclampsia(38%), 17% patients in our study had eclampsia and 4% had pre-eclampsia superimposed on chronic hypertension.

The mean gestational age in (weeks) of the neonates born to subjects in our study was 36.18wks.

In our study there is significant weak negative correlation between serum LDH and gestational age at the time of delivery.

The mean birth weight of the neonates of the subjects in our study was 2.33kg

In our study,there is significant moderate negative correlation between S.LDH and birth weight of neonates.

Association of severity of PIH with serum LDH was significant in our study(p value=0.003)

In our study the mean serum LDH in non severe preclampsia is 440.62 and in severe preclampsia is 522.

- There is significant association between raised serum LDH values and presence of maternal complications in our study.In the study, increase in serum LDH levels was associated with poor maternal outcome in terms of complications,ICU stay and mortality,which was significant(p value=0.00001).
- There were 2 maternal mortality in present study who had serum LDH level 1100U/L and 828U/L respectively.
- In present study,as the number of maternal complications increase the value of serum LDH also increases(p value=0.006)
- In our study, among the patients with
 - 1) serum LDH <360U/L (19 patients)- 3 patients had eclampsia and noneofthepatientshadcomplicationslikeHELLP syndrome, acute renal failure, pulmonary edema and cortical vein thrombosis.
 - 2)serumLDH360-600U/L(62patients), -11 patients had ICU admission,2 had hypertensive retinopathy,8 patients had eclampsia , 2 had abruption placenta, 6 had HELLP syndrome ,1 developed DIC and none of the patient had other complications like acute renal failure or mortality.
 - 3)serumLDH> 600U/L(19 patients)-18 patients had ICU admission,3 had hypertensive retinopathy, 6 had eclampsia ,4 patientshadabruptionplacenta,2hadacuterrenal failure, 3 had pulmonary edema and 5 had HELLPsyndrome.

SERUM LDH AND NEONATAL COMPLICATIONS

- In the present study, out of the 102 neonates born(2 twins) there were 6 still births. 36 required NICU Admission that is developed complications. 16 neonates were premature requiring NICU admission with low birth weight,3 neonates were full term LBW i.e.IUGR.8 had neonatal jaundice,and 6 had meconium stained liquor out of

which 6 developed asphyxia. 2 had only birth asphyxia due to other reasons and 1 had TGA. In our study there is significant association between raised serum LDH values with presence of neonatal complications (p value=0.006)

CONCLUSION:

Preeclampsia and its complications significantly contribute to maternal and perinatal mortality and morbidity. Timely intervention and management can prevent the complications. From this study, after analysing the data, it is found that there is an increase in severity as well as an increase in incidence of maternal and perinatal complications with an increase in serum Lactate dehydrogenase levels in HDP. Thus it is concluded that serum lactate dehydrogenase, which is an early marker of hypoxia at cellular levels, can be used as a biochemical marker to assess the severity of the disease and to predict the complications in all HDP patients. Thereby, close monitoring and early intervention and prompt management of the HDP patients with elevated serum LDH levels can prevent complications and thereby help to improve the maternal and perinatal outcome in HDP.

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